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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/634,895 | 08/06/2003 | Philippe Despres | 241161US0DIV | 7352 |

22850 7590 02/21/2006

OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

| EXAMINER |
|---|
| CHEN, STACY BROWN |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1648 | |

DATE MAILED: 02/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/634,895 | DESPRES ET AL. | |
| | Examiner | Art Unit | |
| | Stacy B. Chen | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *21 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *3-7,10-14,17-23 and 25-65* is/are pending in the application.

4a) Of the above claim(s) *3-7,10-14,17-23,25-41,44-49 and 51-65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42,43 and 50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/6/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Alignment*.

## DETAILED ACTION

1. Applicant's election with traverse of Group VI, claims 42, 43 and 50, is acknowledged. Applicant argues that searching all of the claims of the invention would not be burdensome. In response to this argument, the restriction requirement establishes the distinctness of the inventions and the reasons why a search would be burdensome. Applicant has not specifically addressed any of the particular reasons set forth in the restriction requirement. Applicant also states that if the product claims are allowable, methods relating to the allowable product may be rejoined. In response, the Office recognizes Applicant's right to rejoinder should the elected product claims be found allowable, and if the appropriate method claims relating to such an allowable product are amended during prosecution to correspond with the allowable product. Therefore, the restriction is deemed proper and made FINAL.

Claims 3-7, 10-14, 17-23 and 25-65 are pending. Claims 3-7, 10-14, 17-23, 25-41, 44-49 and 51-65 are withdrawn from consideration being drawn to non-elected subject matter. Claims 42, 43 and 50 are under examination.

### *Specification*

2. The first line of the first page of the specification should be updated to reflect the current status of parent application, USSN 09/881,710, now US Patent 6,673,895.

### *Claim Objections*

3. Claim 50 is objected to for improper grammar in the phrase, "a physiological acceptable carrier", which should be, "a physiologically acceptable carrier". Correction is required.

***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 42, 43 and 50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 42 recites, "An isolated polypeptide of the sequence in SEQ ID NO: 3". The scope of the claim and its dependent claims 43 and 50, is not clear because the claim language could read on fragments of SEQ ID NO: 3. If Applicant intends to claim the full-length sequence of SEQ ID NO: 3, then the following language is suggested for clarity: "An isolated polypeptide comprising SEQ ID NO: 3". Without further explanation in the specification, the claim language fails to convey the metes and bounds of the invention.

Claims 43 and 50 recite the limitation "the peptide of Claim 42". There is insufficient antecedent basis for this limitation in claim 42, which refers only to a polypeptide, not a peptide. Correction is required.

5. Claim 42 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 42 is drawn to an isolated polypeptide comprising SEQ ID NO: 3, wherein said peptide

(polypeptide) induces apoptosis in a cell. The claim encompasses a large genus of cells that are susceptible to apoptosis.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only information provided about the cell is that it is susceptible to apoptosis. However, there is no explanation of how the claimed polypeptide induces apoptosis in the cell, so there is inadequate structure/function correlation. While Applicant has suggested that cancer cells may be a potential target, there are many types of cancer cells. Without further disclosure, Applicant has failed to adequately demonstrate possession of the large genus of cells that are susceptible to apoptosis when somehow contacted with SEQ ID NO: 3. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. It is suggested that the intended function (or inherent function) recited in claim 43 be removed to overcome this rejection.

## *Claim Rejections - 35 USC § 102*

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 42 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Bhamarapravati *et al.* (WO 96/40933, "Bhamarapravati"). The claims are drawn to an isolated polypeptide comprising SEQ ID NO: 3. A reasonable interpretation of the claim language suggests that fragments of SEQ ID NO: 3 are also an embodiment of the invention (see 112, 2nd paragraph rejection above). The polypeptide is capable of inducing apoptosis in a cell.

Bhamarapravati teaches the use of infectious Dengue 2 virus PDK-53 as a quadravalent vaccine. Particularly, a deduced amino acid fragment of Bhamarapravati's SEQ ID NO: 2 (amino acids 211-240) shares 100% sequence identity to Applicant's SEQ ID NO: 3 (see attached Sequence Alignment). While the sequence of Bhamarapravati is larger than Applicant's (3,391 amino acids compared to 30 amino acids), the open claim language reasonably encompasses polypeptides of greater length. Since the structure of Bhamarapravati's polypeptide meets the limitations of the instant claims as written, any inherent functions of the claimed polypeptide are expected to be present in Bhamarapravati's polypeptide. Therefore, claims 42 and 43 are anticipated by the prior art.

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 42, 43 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bhamarapravati *et al.* (WO 96/40933, "Bhamarapravati"). The claims are drawn to an isolated

polypeptide comprising SEQ ID NO: 3. A reasonable interpretation of the claim language suggests that fragments of SEQ ID NO: 3 are also an embodiment of the invention (see 112, 2nd paragraph rejection above). The polypeptide is capable of inducing apoptosis in a cell. Also claimed is a composition comprising SEQ ID NO: 3, or sequence within SEQ ID NO: 3, along with a physiologically acceptable carrier.

Bhamarapravati teaches the use of infectious Dengue 2 virus PDK-53 as a quadravalent vaccine. Particularly, a deduced amino acid fragment of Bhamarapravati's SEQ ID NO: 2 (amino acids 211-240) shares 100% sequence identity to Applicant's SEQ ID NO: 3 (see attached Sequence Alignment). While the sequence of Bhamarapravati is larger than Applicant's (3,391 amino acids compared to 30 amino acids), the open claim language reasonably encompasses polypeptides of greater length. Since the structure of Bhamarapravati's polypeptide meets the limitations of the instant claims as written, any inherent functions of the claimed polypeptide are expected to be present in Bhamarapravati's polypeptide.

While Bhamarapravati suggests the use of the claimed polypeptide in a vaccine, no specific mention of a physiologically acceptable carrier is made. However, one of ordinary skill in the art would have been motivated to use a physiologically acceptable carrier along with the administration of Bhamarapravati's composition. One would have had a reasonable expectation of success that a physiologically acceptable carrier would have worked with Bhamarapravati's composition because the polynucleotide and encoded polypeptide must be administered in some sort of vehicle, even water. Therefore, the invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

***Conclusion***

8. No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James C. Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Stacy B. Chen
February 16, 2006

-Sequence Alignment —

GenCore version 5.1.6


OM protein - protein search, using sw model

Run on: January 4, 2006, 18:32:23 ; Search time 186 Seconds
(without alignments)
70.868 Million cell updates/sec

Title: US-10-634-895-3
Perfect score: 172
Sequence: 1 PHVGMGLETRTETWMSSEGAWKHVQRIETW 30

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 2443163 seqs, 439378781 residues

Total number of hits satisfying chosen parameters: 2443163

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : A_Geneseq_21:*
1: geneseqp1980s:*
2: geneseqp1990s:*
3: geneseqp2000s:*
4: geneseqp2001s:*
5: geneseqp2002s:*
6: geneseqp2003as:*
7: geneseqp2003bs:*
8: geneseqp2004s:*
9: geneseqp2005s:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

| Result No. | Score | % Query Match | Length | DB | ID | Description |
|---|---|---|---|---|---|---|
| 1 | 172 | 100.0 | 48 | 5 | AAE17433 | Aae17433 (95-114)E |
| 2 | 172 | 100.0 | 48 | 9 | ADW12588 | Adw12588 p(95-114) |
| 3 | 172 | 100.0 | 685 | 6 | ABP57874 | Abp57874 Plasmid p |
| 4 | 172 | 100.0 | 685 | 6 | ABP57876 | Abp57876 Plasmid p |
| 5 | 172 | 100.0 | 685 | 6 | ABP57875 | Abp57875 Plasmid p |
| 6 | 172 | 100.0 | 3391 | 2 | AAW06591 | Aaw06591 Polyprote |
| 7 | 172 | 100.0 | 3391 | 2 | AAW06590 | Aaw06590 Polyprote |
| 8 | 172 | 100.0 | 3391 | 4 | AAE07987 | Aae07987 Attenuate |
| 9 | 172 | 100.0 | 3391 | 4 | AAE07986 | Aae07986 Wild-type |
| 10 | 169 | 98.3 | 3391 | 2 | AAR13166 | Aar13166 Proteins |
| 11 | 168 | 97.7 | 40 | 5 | AAE17432 | Aae17432 Dengue (D |
| 12 | 168 | 97.7 | 167 | 8 | ADN37497 | Adn37497 Dengue vi |
| 13 | 168 | 97.7 | 171 | 8 | ADN37493 | Adn37493 Dengue vi |
| 14 | 168 | 97.7 | 171 | 8 | ADN37496 | Adn37496 Dengue vi |
| 15 | 168 | 97.7 | 635 | 2 | AAW75410 | Aaw75410 Fusion pr |
| 16 | 168 | 97.7 | 675 | 8 | ADN37518 | Adn37518 Dengue vi |
| 17 | 168 | 97.7 | 677 | 2 | AAW75411 | Aaw75411 Fusion pr |
| 18 | 168 | 97.7 | 677 | 8 | ADN37613 | Adn37613 Dengue vi |
| 19 | 168 | 97.7 | 681 | 8 | ADN37603 | Adn37603 Dengue vi |
| 20 | 168 | 97.7 | 681 | 8 | ADN37517 | Adn37517 Dengue vi |
| 21 | 168 | 97.7 | 1127 | 2 | AAW09409 | Aaw09409 Dengue vi |
| 22 | 168 | 97.7 | 1127 | 2 | AAY05522 | Aay05522 Dengue vi |
| 23 | 168 | 97.7 | 1127 | 7 | ADL98086 | Adl98086 Dengue vi |
| 24 | 168 | 97.7 | 1127 | 8 | ADQ28716 | Adq28716 Dengue vi |
| 25 | 168 | 97.7 | 3388 | 6 | AAE35314 | Aae35314 Dengue vi |
| 26 | 168 | 97.7 | 3391 | 8 | ADG93314 | Adg93314 DEN2 (Ton |
| 27 | 163 | 94.8 | 678 | 8 | ADN37623 | Adn37623 Dengue vi |
| 28 | 162 | 94.2 | 150 | 1 | AAP91166 | Aap91166 PUO-218 s |
| 29 | 162 | 94.2 | 661 | 4 | AAB84901 | Aab84901 Dengue-2 |
| 30 | 160 | 93.0 | 677 | 8 | ADN37720 | Adn37720 Dengue vi |
| 31 | 159 | 92.4 | 675 | 8 | ADN37628 | Adn37628 Dengue vi |
| 32 | 159 | 92.4 | 675 | 8 | ADN37616 | Adn37616 Dengue vi |
| 33 | 159 | 92.4 | 675 | 8 | ADN37618 | Adn37618 Dengue vi |
| 34 | 159 | 92.4 | 675 | 8 | ADN37612 | Adn37612 Dengue vi |
| 35 | 159 | 92.4 | 675 | 8 | ADN37615 | Adn37615 Dengue vi |
| 36 | 159 | 92.4 | 675 | 8 | ADN37626 | Adn37626 Dengue vi |
| 37 | 159 | 92.4 | 677 | 8 | ADN37617 | Adn37617 Dengue vi |
| 38 | 159 | 92.4 | 3396 | 2 | AAR43662 | Aar43662 DEN1-S275 |
| 39 | 157.5 | 91.6 | 39 | 9 | ADW12576 | Adw12576 M1-40/DEN |
| 40 | 157.5 | 91.6 | 39 | 9 | ADW12582 | Adw12582 M1-40/DEN |
| 41 | 157.5 | 91.6 | 39 | 9 | ADW12599 | Adw12599 M1-40/DEN |
| 42 | 157 | 91.3 | 774 | 8 | ADG93320 | Adg93320 DEN1 (Pue |
| 43 | 157 | 91.3 | 775 | 8 | ADG93318 | Adg93318 DEN1 (Pue |
| 44 | 156 | 90.7 | 39 | 5 | AAE17440 | Aae17440 Dengue vi |
| 45 | 156 | 90.7 | 40 | 5 | AAE17431 | Aae17431 Dengue (D |

ALIGNMENTS

RESULT 1
AAE17433
ID AAE17433 standard; protein; 48 AA.
XX
AC AAE17433;
XX
DT 18-APR-2002 (first entry)
XX
DE (95-114)EGFP(206-245)DEN-2 fusion protein.
XX
KW Dengue virus; pRM glycoprotein; E glycoprotein; apoptosis; virucide;
KW cancer; flavivirus infection; cytostatic; EGFP; DEN-2 protein;
KW enhanced green fluorescent protein; fusion protein; M ectodomain.
XX
OS Dengue virus; 2.
OS Dengue virus; 1.
OS Unidentified.
OS Chimeric.
XX
FH Key Location/Qualifiers
FT Misc-difference 13. .44
FT /note= "Encoded by GTTATC"
XX
PN WO200196376-A2.
XX
PD 20-DEC-2001.
XX
PF 18-JUN-2001; 2001WO-IB001570.
XX
PR 16-JUN-2000; 2000US-0212129P.
XX
PA (INSP ) INST PASTEUR.
XX
PI Despres P, Courageot M, Deubel V, Catteau A;
XX
DR WPI; 2002-139706/18.
DR N-PSDB; AAD27335.
XX
PT Novel apoptosis inducing polypeptide fragments of Dengue virus-1 or 2 M
PT protein, useful for inducing apoptosis in a cell of a human patient
PT suffering from cancer or flavivirus infection.
XX
PS Claim 42; Fig 11; 45pp; English.
XX
CC The invention relates to pro-apoptotic fragments of the Dengue virus
CC (DEN) pRM and E glycoproteins, methods for screening molecules capable of
CC inducing apoptosis and methods of inducing apoptosis in a cell. The

```
Qy          1 PHVGMGLETRTETWMSSEGAWKHVQRIETW 30
              |||||||||||||||||||||||||||||||
Db        121 PHVGMGLETRTETWMSSEGAWKHVQRIETW 150
```

RESULT 4
ABP57876
ID  ABP57876 standard; protein; 685 AA.
XX
AC  ABP57876;
XX
DT  07-FEB-2003  (first entry)
XX
DE  Plasmid pCB8D2-2J-2-9-1 protein product.
XX
KW  Flavivirus; immunogenic flavivirus antigen; virucide; vaccine; prM-E;
KW  pCB8D2-2J-2-9-1; Japanese encephalitis virus; dengue-2 virus; DEN-2.
XX
OS  Unidentified.
OS  Synthetic.
XX
PN  WO200281754-A1.
XX
PD  17-OCT-2002.
XX
PF  04-APR-2002; 2002WO-US010764.
XX
PR  04-APR-2001; 2001US-00826115.
XX
PA  (USSH ) US DEPT HEALTH & HUMAN SERVICES.
XX
PI  Chang GJ;
XX
DR  WPI; 2003-058572/05.
DR  N-PSDB; ABV77549.
XX
PT  Novel isolated nucleic acid useful as vaccine for preventing flavivirus
PT  infection, comprises transcriptional unit encoding signal sequence of one
PT  flavivirus and immunogenic flavivirus antigen of a second flavivirus.
XX
PS  Example 20; Page 168-169; 174pp; English.
XX
CC  The invention relates to a novel nucleic acid comprising a
CC  transcriptional unit encoding a signal sequence of a structural protein
CC  of a first flavivirus and an immunogenic flavivirus antigen of a second
CC  flavivirus, where the transcriptional unit directs the synthesis of the
CC  antigen. The polynucleotide of the invention has virucide activity, and
CC  acts as a vaccine. A composition of the invention is useful for
CC  immunising a subject against infection by a flavivirus. The
CC  polynucleotide is useful as a vaccine for preventing flavivirus
CC  infection. The sequence represents plasmid pCB8D2-2J-2-9-1, which
CC  contains dengue-2 virus (DEN-2) prM, M and E, and Japanese encephalitis
CC  virus E proteins
XX
SQ  Sequence 685 AA;

```
  Query Match             100.0%;  Score 172;  DB 6;  Length 685;
  Best Local Similarity   100.0%;  Pred. No. 2.7e-16;
  Matches   30;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 PHVGMGLETRTETWMSSEGAWKHVQRIETW 30
              |||||||||||||||||||||||||||||||
Db        121 PHVGMGLETRTETWMSSEGAWKHVQRIETW 150
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RESULT 5
ABP57875
ID  ABP57875 standard; protein; 685 AA.
XX
AC  ABP57875;
XX
DT  07-FEB-2003  (first entry)
XX
DE  Plasmid pCB9D2-IJ-4-3 protein product.
XX
KW  Flavivirus; immunogenic flavivirus antigen; virucide; vaccine; prM-E;
KW  pCB9D2-IJ-4-3; Japanese encephalitis virus; dengue-2 virus; DEN-2.
XX
OS  Unidentified.
OS  Synthetic.
XX
PN  WO200281754-A1.
XX
PD  17-OCT-2002.
XX
PF  04-APR-2002; 2002WO-US010764.
XX
PR  04-APR-2001; 2001US-00826115.
XX
PA  (USSH ) US DEPT HEALTH & HUMAN SERVICES.
XX
PI  Chang GJ;
XX
DR  WPI; 2003-058572/05.
DR  N-PSDB; ABV77548.
XX
PT  Novel isolated nucleic acid useful as vaccine for preventing flavivirus
PT  infection, comprises transcriptional unit encoding signal sequence of one
PT  flavivirus and immunogenic flavivirus antigen of a second flavivirus.
XX
PS  Example 20; Page 162-164; 174pp; English.
XX
CC  The invention relates to a novel nucleic acid comprising a
CC  transcriptional unit encoding a signal sequence of a structural protein
CC  of a first flavivirus and an immunogenic flavivirus antigen of a second
CC  flavivirus, where the transcriptional unit directs the synthesis of the
CC  antigen. The polynucleotide of the invention has virucide activity, and
CC  acts as a vaccine. A composition of the invention is useful for
CC  immunising a subject against infection by a flavivirus. The
CC  polynucleotide is useful as a vaccine for preventing flavivirus
CC  infection. The sequence represents plasmid pCB9D2-IJ-4-3, which contains
CC  dengue-2 virus (DEN-2) prM, M and E, and Japanese encephalitis virus E
CC  proteins
XX
SQ  Sequence 685 AA;

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  Query Match             100.0%;  Score 172;  DB 6;  Length 685;
  Best Local Similarity   100.0%;  Pred. No. 2.7e-16;
  Matches   30;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 PHVGMGLETRTETWMSSEGAWKHVQRIETW 30
              |||||||||||||||||||||||||||||||
Db        121 PHVGMGLETRTETWMSSEGAWKHVQRIETW 150
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RESULT 6
AAW06591
ID  AAW06591 standard; protein; 3391 AA.
XX
AC  AAW06591;
XX
DT  27-AUG-2003  (revised)
DT  12-SEP-1997  (first entry)
XX
DE  Polyprotein of attenuated DEN-2 virus, strain 16681, PDK-53.
XX
KW  Dengue 2 virus; polyprotein; capsid; prM; M; E; NS1; NS2A; NS2B; NS3;
KW  NS4A; NS4B; NS5; PDK-53; quadravalent vaccine; immunity; serotype;
KW  chimeric DEN-2/1 virus; chimeric DEN-2/3 virus; chimeric DEN-2/4 virus;
KW  dengue fever; fatal dengue haemorrhagic fever; dengue shock syndrome;
KW  DHF; DSS.
XX
OS  Dengue virus type 2 (strain 16681).
XX
FH  Key             Location/Qualifiers
FT  Protein         2. .114

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FT                   /label= Capsid_protein
FT   Protein         115. .205
FT                   /label= prM
FT   Modified-site   183
FT                   /note= "N-linked glycosylation site, encoded by NAC"
FT   Protein         206. .280
FT                   /label= M
FT   Protein         281. .775
FT                   /label= E
FT   Modified-site   347
FT                   /note= "N-linked glycosylation site, encoded by NAC"
FT   Modified-site   433
FT                   /note= "N-linked glycosylation site, encoded by NAT"
FT   Protein         776. .1127
FT                   /label= NS1
FT   Modified-site   905
FT                   /note= "N-linked glycosylation site, encoded by NAC"
FT   Modified-site   982
FT                   /note= "N-linked glycosylation site, encoded by NAT"
FT   Protein         1128. .1345
FT                   /label= NS2A
FT   Protein         1346. .1475
FT                   /label= NS2B
FT   Protein         1476. .2093
FT                   /label= NS3
FT   Protein         2094. .2242
FT                   /label= NS4A
FT   Protein         2243. .2491
FT                   /label= NS4B
FT   Protein         2492. .3391
FT                   /label= NS5
FT   Misc-difference 3038
FT                   /note= "Encoded by KKA"
XX
PN   WO9640933-A1.
XX
PD   19-DEC-1996.
XX
PF   06-JUN-1996;   96WO-US009209.
XX
PR   07-JUN-1995;   95US-00483292.
XX
PA   (USSH ) US DEPT HEALTH & HUMAN SERVICES.
PA   (UYMA-) UNIV MAHIDOL AT SALAYA.
XX
PI   Bhamarapravati N,  Butrapet S,  Chang J,  Gubler DJ,  Halstead SB;
PI   Kinney R,  Trent DW;
XX
DR   WPI; 1997-052330/05.
DR   N-PSDB; AAT49304.
XX
PT   PDK-53, a clone of infectious attenuated Dengue 2 virus strain 16681 -
PT   also chimeric DEN-2/1, DEN-2/3 and DEN-1/4 viruses, used as a
PT   quadravalent vaccine for protecting against Dengue virus infection.
XX
PS   Claim 27; Page 122-136; 261pp; English.
XX
CC   This sequence represents the polyprotein from attenuated Dengue 2 virus,
CC   strain 16681. The attenuated virus is designated PDK-53. The poly-
CC   protein comprises the capsid, prM, M, E, NS1, NS2A, NS2B, NS3, NS4A, NS4B
CC   and NS5 proteins. A clone of this wildtype viral sequence, PDK-53, may be
CC   used in the production of a quadravalent vaccine which provides immunity
CC   against all four serotypes of dengue virus. The vaccine also comprises a
CC   chimeric DEN-2/1 virus, a chimeric DEN-2/3 virus, and/or a chimeric DEN-
CC   2/4 virus. The new quadravalent vaccines are used to protect against
CC   infection by all four serotypes of dengue virus, DEN-1, DEN-2, DEN-3 and
CC   DEN-4, which can lead to dengue fever or fatal dengue haemorrhagic
CC   fever/dengue shock syndrome (DHF/DSS). Host cells are used to produce the
CC   recombinant protein products of the DNA constructs which are used in the
CC   vaccines. (Updated on 27-AUG-2003 to correct OS field.)
XX
SQ   Sequence 3391 AA;
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  Query Match            100.0%;  Score 172;  DB 2;  Length 3391;
  Best Local Similarity  100.0%;  Pred. No. 1.8e-15;
  Matches   30;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

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              ||||||||||||||||||||||||||||||
Db        211 PHVGMGLETRTETWMSSEGAWKHVQRIETW 240
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RESULT 7
AAW06590
ID   AAW06590 standard; protein; 3391 AA.
XX
AC   AAW06590;
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DT   27-AUG-2003  (revised)
DT   11-SEP-1997  (first entry)
XX
DE   Polyprotein of DEN-2 virus, strain 16681.
XX
KW   Dengue 2 virus; polyprotein; capsid; prM; M; E; NS1; NS2A; NS2B; NS3;
KW   NS4A; NS4B; NS5; PDK-53; quadravalent vaccine; immunity; serotype;
KW   chimeric DEN-2/1 virus; chimeric DEN-2/3 virus; chimeric DEN-2/4 virus;
KW   dengue fever; fatal dengue haemorrhagic fever; dengue shock syndrome;
KW   DHF; DSS.
XX
OS   Dengue virus type 2 (strain 16681).
XX
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FT                   /label= Capsid_protein
FT   Protein         115. .205
FT                   /label= prM
FT   Modified-site   183
FT                   /note= "N-linked glycosylation site"
FT   Protein         206. .280
FT                   /label= M
FT   Protein         281. .775
FT                   /label= E
FT   Modified-site   347
FT                   /note= "N-linked glycosylation site"
FT   Modified-site   433
FT                   /note= "N-linked glycosylation site"
FT   Protein         776. .1127
FT                   /label= NS1
FT   Modified-site   905
FT                   /note= "N-linked glycosylation site"
FT   Modified-site   982
FT                   /note= "N-linked glycosylation site"
FT   Protein         1128. .1345
FT                   /label= NS2A
FT   Protein         1346. .1475
FT                   /label= NS2B
FT   Protein         1476. .2093
FT                   /label= NS3
FT   Protein         2094. .2242
FT                   /label= NS4A
FT   Protein         2243. .2491
FT                   /label= NS4B
FT   Protein         2492. .3391
FT                   /label= NS5
FT   Misc-difference 3038
FT                   /note= "Encoded by KKA"
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PN   WO9640933-A1.
XX
PD   19-DEC-1996.
XX
PF   06-JUN-1996;   96WO-US009209.
XX
PR   07-JUN-1995;   95US-00483292.
XX
PA   (USSH ) US DEPT HEALTH & HUMAN SERVICES.
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